

1. A purified nucleic acid comprising a region that hybridizes under high stringency conditions to a probe comprising at least 75 consecutive nucleotides that are complementary to a portion of an *n-sad* gene, wherein said region comprises at least 75 consecutive nucleotides.

5 2. The nucleic acid of claim 1, wherein said *n-sad* gene is a *Pseudomonas fluorescens* *sad* gene, and wherein said *Pseudomonas fluorescens* *sad* gene comprises a sequence chosen from SEQ ID NOs: 1-24.

3. The nucleic acid of claim 1, wherein said nucleic acid is contained within an expression vector.

10 4. The nucleic acid of claim 1, wherein said nucleic acid encodes a polypeptide that has a biological activity necessary for biofilm formation under at least one condition known to allow biofilm formation by a bacterium that expresses said polypeptide.

15 5. A probe comprising at least 18 nucleotides that are complementary to an *n-sad* gene, wherein said *n-sad* gene is a *Pseudomonas fluorescens* *n-sad* gene, wherein said *Pseudomonas fluorescens* *n-sad* gene comprises a sequence chosen from SEQ ID NOs: 1-24.

20 6. The probe of claim 5, wherein said probe comprises at least 25, 40, 60, 80, 120, 150, 175, or 200 nucleotides that are complementary to said *n-sad* gene.

7. A substantially pure *n-sad* polypeptide.

8. The polypeptide of claim 7, wherein said polypeptide has a biological activity necessary for biofilm formation under at least one condition known to allow biofilm formation by a bacterium that expresses said polypeptide.

5 9. A substantially pure antibody that specifically binds an *n-sad* polypeptide.

10 10. The polypeptide of claim 7 or 9, wherein said polypeptide comprises a polypeptide encoded by a *Pseudomonas fluorescens n-sad* gene, wherein said *Pseudomonas fluorescens n-sad* gene comprises a sequence chosen from SEQ ID NOS: 1-24.

11. A method of screening for a compound that modulates biofilm formation, said method comprising:

a) contacting a sample with a test compound, wherein said sample contains a *sad* gene, a *sad*/reporter gene, or a *sad* polypeptide, and

15 b) measuring the level of *sad* biological activity in said sample, wherein an increase in *sad* biological activity in said sample, relative to *sad* biological activity in a sample not contacted with said test compound, indicates a compound that increases biofilm formation, and a decrease in *sad* biological activity in said sample, relative to *sad* biological activity in a sample not contacted with said test compound, indicates a compound that decreases biofilm formation.

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12. The method of claim 11, wherein said sample comprises bacterial cell extract.

13. The method of claim 11, wherein said *sad* gene, said *sad*/reporter gene, or said *sad* polypeptide is within a bacterial cell.

5 14. The method of claim 11, wherein said *sad* gene, said *sad*/reporter gene, and said *sad* polypeptide are from *Pseudomonas fluorescens*, wherein said *sad* gene and said *sad*/reporter gene comprise a sequence chosen from SEQ ID NOS: 1-24, and wherein said *sad* polypeptide is encoded by a gene comprising a sequence chosen from SEQ ID NOS: 1-24.

10 15. A method of screening for a compound that modulates biofilm formation, said method comprising:

a) contacting a sample with a test compound, wherein said sample contains a *clpP* gene, a *clpP*/reporter gene, or a ClpP polypeptide, and

15 b) measuring the level of ClpP activity in said sample, wherein an increase in ClpP activity in said sample, relative to ClpP activity in a sample not contacted with said test compound, indicates a compound that increases biofilm formation, and a decrease in ClpP activity in said sample, relative to ClpP activity in a sample not contacted with said test compound, indicates a compound that decreases biofilm formation.

20 16. The method of claim 15, wherein said *clpP* gene, said *clpP*/reporter gene, or said ClpP polypeptide is a non-*E. coli* *clpP* gene, a non-*E. coli* *clpP*/reporter gene, or a non-*E. coli* ClpP polypeptide.

17. The method of claim 15, wherein said sample comprises bacterial cell extract.

18. The method of claim 15, wherein said *clpP* gene, said *clpP*/reporter gene, or said ClpP polypeptide is within a bacterial cell.

5 19. The method of claim 18, wherein said bacterial cell is cultured under standard biofilm assay conditions after said contacting.

20. The method of claim 15, wherein said *clpP* gene, said *clpP*/reporter gene, or said ClpP polypeptide is from *Pseudomonas fluorescens*.

10 21. The method of claim 15, wherein ClpP activity is measured by measuring biofilm formation.

22. A method for preventing a bacterial cell from participating in formation of a biofilm, said method comprising a step selected from the group consisting of: inhibiting the synthesis or function of a *sad* polypeptide; inhibiting protein synthesis in said bacterial cell; contacting said bacterial cell with a 15 protease, wherein said contacting is sufficient to prevent said bacterial cell from participating in formation of a biofilm; limiting the concentration of  $Fe^{2+}/Fe^{3+}$  in the environment of said bacterial cell, wherein the  $Fe^{2+}/Fe^{3+}$  concentration in said environment is limited to 0.3  $\mu M$  or less; providing a high osmolarity environment to said bacterial cell, wherein said osmolarity of said environment is 20 equivalent to or greater than the osmolarity of a solution containing 0.2 M NaCl or 15% sucrose; adding mannose to the environment of said bacterial cell, such that the mannose concentration in said environment after the addition of said

mannose is at least 15 mM; and adding  $\alpha$ -methyl-D-mannoside to the environment of said bacterial cell, such that the  $\alpha$ -methyl-D-mannoside concentration in said environment after the addition of said  $\alpha$ -methyl-D-mannoside is at least 15 mM.

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23. The method of claim 22, wherein *sad* polypeptide is encoded by a *Pseudomonas fluorescens* *sad* gene.

24. The method of claim 22, wherein said mannose concentration or said  $\alpha$ -methyl-D-mannoside concentration is at least 15 mM, 25 mM, 50 mM, or 10 100 mM.

25. The method of claim 22, wherein said surface is an abiotic surface.

26. The method of claim 13, 18, or 22, wherein said bacterial cell is selected from the group including: *Pseudomonas fluorescens*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Vibrio parahaemolyticus*, *Salmonella typhimurium*, *Streptococcus mutans*, *Enterococcus* species, *Serratia marcescens*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus hominis*, *Staphylococcus haemolyticus*, *Staphylococcus warneri*, *Staphylococcus cohnii*, *Staphylococcus saprophyticus*, *Staphylococcus capitis*, and *Staphylococcus lugdunensis*.

27. A method for inhibiting participation of a bacterium in formation of a biofilm on a surface, said method comprising inhibiting the synthesis or function of a flagellum on said bacterium.

28. The method of claim 27, wherein said surface is abiotic.

29. The method of claim 27, wherein said synthesis or function of said flagellum is inhibited by inhibiting the synthesis or function of: FliC (SEQ ID NO: 34); FlhD (SEQ ID NO: 35); MotA (SEQ ID NO: 36); MotB (SEQ ID NO: 37); FliP (SEQ ID NO: 38); FlaE (AB 001340; SEQ ID NO: 39); or FlgK (SEQ ID NO: 40); or homologues thereof.

30. A method for inhibiting participation of a bacterium in formation of a biofilm on an abiotic surface, said method comprising inhibiting the synthesis or function of a pilus on said bacterium.

10 31. The method of claim 30, wherein said function of said pilus is inhibited by contacting said pilus with mannose or  $\alpha$ -methyl-D-mannoside.

15 32. The method of claim 30, wherein said synthesis or said function of said pilus is inhibited by inhibiting the synthesis or function of: PilB (SEQ ID NO: 41); PilC (SEQ ID NO: 42); PilD (SEQ ID NO: 43); PilV (SEQ ID NO: 44); PilW (SEQ ID NO: 45); PilX (SEQ ID NO: 46); PilY1 (SEQ ID NO: 47); PilY2 (SEQ ID NO: 48); or PilE (SEQ ID NO: 49); or homologues thereof.

20 33. The method of claim 30, wherein said bacterium is chosen from the group including: *Pseudomonas fluorescens*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Vibrio paramaemolyticus*, *Salmonella typhimurium*, *Streptococcus mutans*, *Enterococcus* species, *Serratia marcescens*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus hominis*, *Staphylococcus haemolyticus*, *Staphylococcus warneri*, *Staphylococcus cohnii*,

*Staphylococcus saprophyticus*, *Staphylococcus capitis*, and *Staphylococcus lugdunensis*.

34. A method of screening for a compound that inhibits bacterial pathogenicity, said method comprising:

5           a) exposing a bacterial culture to a test compound, such that at least one bacterial cell in said bacterial culture are contacted by said test compound, and

10           b) testing said bacterial culture for biofilm formation on an abiotic surface, wherein a decrease in biofilm formation, relative to biofilm formation by a bacterial culture that has not been exposed to said test compound, indicates a compound that inhibits biofilm formation, and an increase in biofilm formation, relative to biofilm formation by a bacterial culture that has not been exposed to said test compound, indicates a compound that stimulates biofilm formation.

15           35. The method of claim 34, wherein said bacterial culture is a liquid bacterial culture.

36. The method of claim 34, wherein at least 5%, 10%, 25%, 50%, 75%, or 100% of the bacterial cells contacted by the bacterial growth medium in said culture are contacted by said test compound.

20           37. The method of claim 34, wherein said bacterium is chosen from the group including: *Pseudomonas fluorescens*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Vibrio parahaemolyticus*, *Salmonella typhimurium*, *Streptococcus mutans*, *Enterococcus* species, *Serratia marcescens*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus hominis*,  
25           *Staphylococcus haemolyticus*, *Staphylococcus warneri*, *Staphylococcus cohnii*,

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*Staphylococcus saprophyticus*, *Staphylococcus capitis*, and *Staphylococcus lugdunensis*.

38. A method of stimulating formation of a biofilm by a population of bacteria, said method comprising at least one of: adding iron to the growth environment of said bacteria, such that the final concentration of said iron in said growth environment is at least 3  $\mu$ M; adding glutamate to the growth environment of said bacteria, such that the final concentration of said glutamate in said growth environment is at least 0.4%; adding citrate to the growth environment of said bacteria, such that the final concentration of said citrate in said growth environment is at least 0.4%; and stimulating expression of a *sad* gene or activity of a *sad* polypeptide.

39. The method of claim 38, wherein said population comprises *Pseudomonas fluorescens*.